ORIGINAL ARTICLE

Surgical Treatment for Empty Nose Syndrome

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Objectives: To detail empty nose syndrome (ENS), an iatrogenic disorder characterized by a patent airway but a subjective sense of poor nasal breathing, and to explore repair options for patients with ENS.

Design: A case series of 8 patients with ENS detailing symptoms before and after submucosal implantation of acellular dermis.

Setting: Academic medical center.

Patients: Subjects who were evaluated for abnormal nasal breathing and determined to have ENS. Patients were diagnosed as having ENS if they described characteristic symptoms, had evidence of prior nasal turbinate surgery, and their symptoms improved after they underwent a cotton test.

Intervention: Acellular dermis was implanted submucosally to simulate missing turbinate tissue.

Main Outcome Measures: Symptoms and symptom scores for the 20-item Sino-Nasal Outcome Test completed before and after the implantation were gathered.

Results: A statistically significant improvement in symptom scores for the Sino-Nasal Outcome Test was noted ($P \leq .02$).

Conclusions: Careful assessment allows reconstructive surgery through submucosal implantation of acellular dermis. Symptoms of patients with ENS can improve with surgical therapy.

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Over the past 6 years I have sought to better understand the entity termed *empty nose syndrome* (ENS) by engaging in discussions over the Internet with potential patients with ENS.[1] I have evaluated hundreds of symptoms and sinus computed tomographic (CT) scans to screen for ENS. Dozens of patients with ENS from many states and several foreign countries have been seen at MetroHealth Medical Center (Cleveland, Ohio) for a full evaluation of ENS. Eleven patients have undergone nasal submucosal acellular dermis implantation in an effort to rebuild the inside of their nose and to reverse some of their symptoms. This article describes ENS and presents the results of those patients who have undergone submucosal acellular dermis implantation.

It is difficult to diagnose ENS because there are no reliable objective tests. The otolaryngologist must rely on the patient's subjective symptoms to diagnose ENS. It is caused by too much turbinate tissue loss, which is revealed fully by a CT scan. Although perhaps in a milder form, ENS is sometimes seen even in patients who have lost relatively little of their turbinate tissues and whose turbinates appear to be almost normal in size (hereinafter, ENS-type patients); this is especially true in cases of anterior inferior turbinate (IT) resection because of its important role in the internal nasal valve. The rate of occurrence of ENS after turbinectomies is not known. Potentially, many patients with ENS are not diagnosed because most rhinologists are trained to look for physical signs of dryness and atrophy after turbinectomies—the only possible long-term complications—and may thus ignore the patients' subjective complaints of nasal obstruction or shortness of breath. Like many other otolaryngologic disorders (eg, tinnitus), the fact that the symptoms are subjective and cannot be verified objectively does not mean they are not real and valid symptoms originating in a physical abnormality.

Manometric studies or acoustic rhinometry will indicate a fully patent airway that contrasts greatly with the patient's breathing complaints. Such flow studies might denote an overly patent nose with below-normal rates of resistance. When this is accompanied by a CT scan that suggests that a turbinate reductive procedure took place, the physician's suspicion for ENS should be raised; however, the fact that a patient has an overly patent nose does not necessarily mean that he or she has ENS. A healthy nose provides about half of the resistance of the entire respiratory tract. A serious decline in this resistance might considerably upset the balance of resistance needed for deep pulmonary inspiration and result in short-

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ness of breath, just as patients with ENS notice that even though their noses are completely open and air reaches their lungs, they cannot seem to breathe in deeply enough to feel satisfied.[2] It is well known that even though 50% more effort is required to breathe through the nose than through the mouth, nasal breathing is much more satisfying and effective than mouth breathing.[3] Resection of the turbinates, which are the main intranasal structures that provide this much-needed respiratory resistance, makes the nose both less effective and less efficient.

The symptom that most often indicates ENS is paradoxical obstruction: subjects may have an impressively large nasal airway because they lack turbinate tissue, yet they state they feel they cannot breathe well. There is no clear way to describe the breathing sensation that patients with ENS experience. Some patients may state that their nose feels "stuffy," for lack of a better word, whereas others state their nose feels too open, yet they cannot seem to properly inflate the lungs; they feel they need some resistance to do so. Patients with ENS do not sense the airflow passing through their nasal cavities, whereas their distal structures (pharynx, lungs) do detect inspiration; the patients' central nervous systems receive conflicting information. These patients seem to be in a constant state of dyspnea and may describe the sensation of suffocating. The constant abnormal breathing sensations cause these patients to be consistently preoccupied with their breathing and nasal sensations, and this often leads to the inability to concentrate (aprosexia nasalis), chronic fatigue, frustration, irritability, anger, anxiety, and depression. Simple advice to breathe through the mouth is woefully inadequate to overcome these sensations and, quite frankly, disrespectful to the patient. Viscous phlegm, heightened sensitivity to volatile compounds (eg, gasoline, perfume), cold air, and air-borne irritants cause pulmonary irritation and worsen the feeling of dyspnea. Patients with ENS often report a quantitative decrease in their ability to smell, although their qualitative identification of odors remains intact. The greater the impact on the remaining nasal mucosa by dry and cold air, the more it tends to get so irritated and dry that squamous metaplasia takes place. Patients with ENS may develop pharyngitis and laryngitis.[4] They may also develop patulous eustachian tubes. Many of them experience sleep-disordered breathing and tend to snore frequently and switch to oral breathing only. They wake up feeling tired and unrefreshed. Crusting and pain are occasionally components of ENS symptoms as well. In some patients, their tissue loss may progress, and atrophic rhinitis may develop.

My observations lead me to the conclusion that ENS does not occur only when the nasal lining becomes very dry or grossly atrophic, as has been previously implied in the literature,[5] but rather that ENS symptoms are often felt by patients soon after turbinectomy procedures, and these symptoms seem to worsen as years go by and higher levels of dryness and occasionally nasal atrophy set in.

METHODS

This study was reviewed and approved by the MetroHealth Medical Center institutional review board. Eleven subjects underwent surgical procedures, but 3 were lost to follow-up. The ages of the 8 remaining study subjects at the time of submucosal implantation of acellular dermis ranged from 18 to 45 years. One patient was female, and 7 were male. One patient was Asian; 1, Hispanic; and 6, white. The durations of their follow-up ranged from 6 months to 4 years. Patients were asked to express their symptoms as free text and to complete Sino-Nasal Outcome Test (SNOT-20) surveys to assess their symptoms before and after implantation. The postimplantation symptoms were assessed 3 to 6 months after surgery. The SNOT-20 is a validated 20-item survey that examines general nasal symptoms and can be used as a comparator before and after some type of intervention; each item is scored from 0 (no symptoms) to 5 (severe symptoms).[6]

Patients were diagnosed as having ENS based on physical examination and symptoms consistent with ENS: paradoxical airway obstruction, dyspnea, dryness, and often depression. Patients were evaluated for ENS with a head mirror and a zero-degree rigid endoscope with no anesthesia or decongestant that would interfere with a subsequent cotton test. Patients were assigned to subcategories within ENS based on their anatomic characteristics. The designations indicate the type of tissue that was resected; hence "ENS-IT" indicates that the IT was fully or subtotally resected and "ENS-MT" notes a similar insult to the middle turbinate, whereas "ENS-both" indicates both the IT and MT were at least partially resected. Finally, as already described in the second paragraph of this article, "ENS-type" designates patients who appear to have adequate turbinate tissue, yet their concerns seem to fully emulate ENS; they have all undergone some type of turbinate procedure in the past, and they improve with the cotton test. All patients with ENS are treated medically with maximal moisturization (eg, use of a humidifier, isotonic sodium chloride solution spray, emollients) before considering any implantation, and such care is continued afterward according to their subjective dryness concerns. Generally, a patient needs to allow a year to elapse after their last turbinate surgery to await any possible recovery of function before implantation is considered.

During evaluation, a cotton test is performed to gauge the size and location of a potential implant in a particular individual. This test is performed by placing cotton moistened with isotonic sodium chloride solution within the nonanesthetized nasal cavity in a region where an implant would be feasible (eg, along the septum opposite the site of a missing MT). The patient is then asked to breathe comfortably with this in place for approximately 30 minutes and to gauge any change in sensation or symptoms. Multiple pieces of cotton can be placed to aid in planning the size and location of a potential implant. Alternatively, an injection of isotonic sodium chloride solution can be made in the location, although its effects are more fleeting. Patients who report a definite subjective improvement from the cotton test, and whose symptoms and findings from a physical examination seem to be consistent with ENS, are offered submucosal acellular dermis implantation.

Implantation is performed in the operating room under general anesthesia, and acellular dermis (AlloDerm; LifeCell, Branchburg, New Jersey) is used. The ITs of ENS-type patients can be directly expanded in a submucosal layer: a tunnel within the IT tissue can be filled with strips cut from a 1×2-cm extra thick piece of acellular dermis. The nasal septum and/or floor mucosa have been implanted in other patients with ENS subtypes. A submucoperichondrial and submucoperiosteal plane is identified to create a pocket for implantation. In patients with ENS-MT, the implant is carefully positioned endoscopically and sutured into position in the septum opposite the site of the missing MT: usually 2 extra thick 1×2-cm pieces of acellular dermis are rolled at their tip and sutured into position with 4-0 chromic sutures[7] (**Figure 1**). To simulate an IT, the implant is placed at the septum or floor with care to keep the graft sufficiently an-

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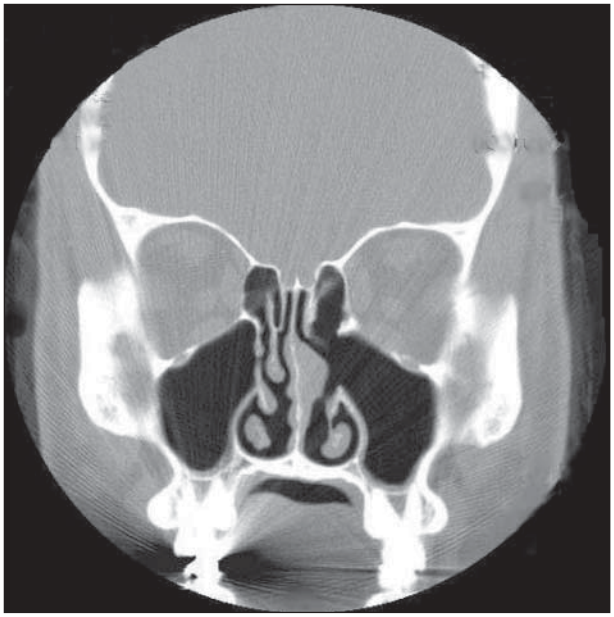

Figure 1. A computed tomographic scan of a septum implanted on the left with acellular dermis.

terior so as to be opposite the former IT head (**Figure 2**). If the graft is placed at the lateral wall, then care is taken to not obstruct the nasolacrimal duct by building up the front of the duct area while minimizing the graft directly below the duct. The volume of acellular dermis used to benefit patients with ENS-IT depends on the volume of missing tissue and the results of their cotton test; often several extra thick 2×4-cm acellular dermis sheets are rolled and closed with 4-0 chromic suture to form a structure to bury in the appropriate pocket. Each pocket is closed with 4-0 chromic suture to keep the acellular dermis graft in position. Strip gauze packing is placed overnight for large implants. The patient receives prophylactic antibiotics (eg, cephalexin hydrochloride, 500 mg, twice a day) for 3 weeks following implantation. The patients were asked to describe their ENS symptoms and fill out SNOT-20 surveys to compare their preimplantation symptoms with postimplantation symptoms.

RESULTS

The **Table** summarizes the findings in the 8 patients who underwent implantation and completed surveys at least 3 months postoperatively. The SNOT-20 symptoms that subjects reported as most troubling before implantation were fatigue, facial pain or pressure, and lack of a good night's sleep; after implantation, the most common persistent concerns were facial pain or pressure and postnasal drip. No new symptoms seemed to develop after implantation. The SNOT-20 values that relate to depression (sadness, irritability, and difficulty sleeping) tended to improve after implantation. Additional symptoms were elicited as free text. Each of these patients reported subjective improvement after implantation, including subject 4, whose SNOT-20 score showed no change. Several patients noted a subjective improvement in their quantitative smell threshold, but this effect was not quantified. The level of dryness subjectively improved in most of the patients who wrote a free-text response. The free-text data have allowed me to create 5 additional questions, beyond the SNOT-20, that are ENS specific for future studies; quantification of more symptoms will be possible in the future. Two patients had some minor exposure of their acellular dermis graft material during the first 2 weeks of healing, but all went on to heal with no sequelae, no infections, and no major complications.

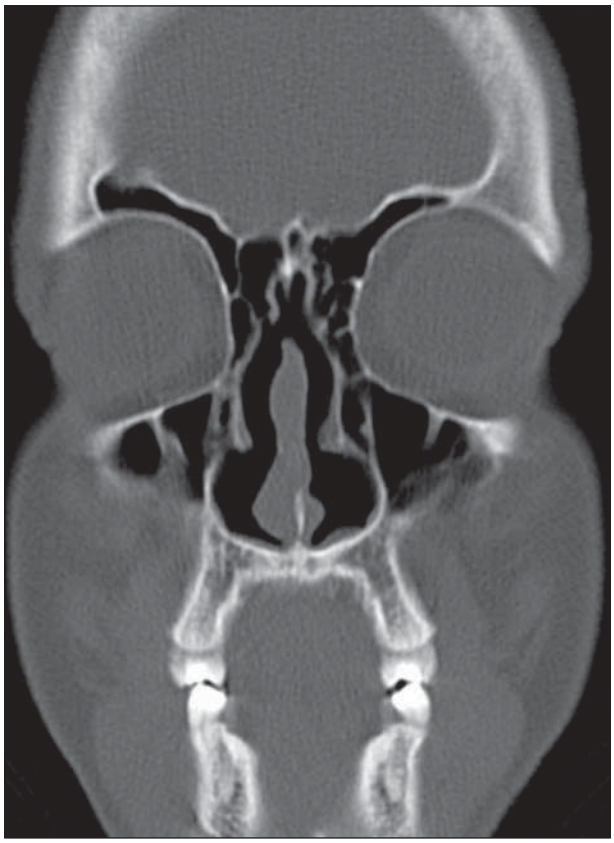

Figure 2. A computed tomographic scan of a right septum region implanted with acellular dermis. The graft was expanded with additional acellular dermis 9 months later.

Because the individual subjects' symptoms were quite varied, a nonparametric statistical method (Wilcoxon signed-rank test) was used to analyze the data. The mean (SD) SNOT-20 score before implantation vs after implantation was 58.3 (16.6) with a median value of 56 vs 38.3 (17.4) with a median value of 37.5. The mean SNOT-20 reduction was statistically significant ($P \leq .02$ for the nondirectional test).

COMMENT

The true incidence rate of ENS is uncertain, but it is known to be a potentially devastating complication of nasal surgery. Passàli et al[8] noted a 22.2% incidence of "atrophy" (likely ENS) following inferior turbinectomy. However, many patients undergo turbinate reduction without apparent adverse effects. Ophir et al[9] reported long-term follow-up after total IT resection without ENS, whereas Moore et al[10] were more critical of the procedure. Even Courtiss and Goldwyn,[11] proponents of partial turbinectomy, noted that 20% of their subjects had no improvement in their symptoms and 8% felt worse; in addition, 8% developed a dry nose. These percentages suggest an incidence of ENS within their surgical population. Most

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Table. Characteristics of the Patients

Case	Prior Surgery	Onset of ENS Symptoms After TS	ENS Subtype[a]	SNOT-20 Score, Preimplantation[b]	Site of Implantation	SNOT-20 Score, Postimplantion	Additional ENS Symptoms	Patients' Postimplantation Comments	Length of Follow-up, y
1	Revision sinus surgery, left MT resection (20% remains), IT cautery	Within days	ENS-MT	54	Septum opposite the MT to treat ENS; into floor in attempt to limit airflow to pain trigger	15	Dryness, pain	Multiple implanted SPs, feels 80% relief of ENS	4.0
2	IT resection (20% remains on left; 40%, on right)	Within months	ENS-IT	93	Left inferior septum and floor; right IT augmented	55	Dryness, difficulty breathing	2 Implanted SPs; patulous ETs; feels 60% improv	3.5
3	Laser turbinate reduction	Within months	ENS-type	62	Bilateral IT augmented	25	Dryness, congestion, feeling of suffocation, voice problems, thick postnasal drip	Feels 80%-90% relief	2.5
4	Septoplasty, sinus surgery, MT resection (20% remains on right; 10%, on left)	Within days	ENS-MT	66	Septal implantation opposite missing MT	66	Pain, feeling of suffocation	2 Implanted SPs; severe facial pain; 5%-10% pain reduction; 0%-25% breathing improv	2.5
5	Laser turbinate reduction	Within 1-2 y	ENS-type	49	Bilateral IT augmented	39	Sleep problems, fatigue, cannot concentrate, difficulty breathing	Feels improv but symptoms fluctuate	1.5
6	Septoplasty, PT (10% remains of right IT; 40%, of left; and 50%, of MT	Within days	ENS-both	45	Right septal implantation	36	Dryness, crust, pressure, and poor breathing	30% improv	0.5
7	Septoplasty, sinus surgery, MT resection (15% of MT remains bilateral)	Within days	ENS-MT	58	Septal implantation opposite missing MT	48	Cough, dryness, difficult to regulate breathing	Feels 25% better	0.5
8	IT trimming, revision rhinoplasty	Within days	ENS-type	39	Bilateral IT augmented; right vestibular implantation	22	Dryness, too open	2 Implanted SPs; less dry; 50% better	2.75

Abbreviations: ENS, empty nose syndrome; ET, eustachian tube; improv, improvement; IT, inferior turbinate; MT, middle turbinate; PT, partial turbinectomy; SNOT-20, 20-item Sino-Nasal Outcome Test; SP, surgical procedure; TS, turbinate surgery.

[a] ENS-type indicates patients who have lost relatively little of their turbinate tissues and whose turbinates appear to be almost normal in size; ENS-both, patients in whom both the IT and MT were at least partially resected.

[b] Scores can range from 0 to 100; each item is scored from 0 (no symptoms) to 5 (severe symptoms).

otolaryngologists accept that ENS exists and that turbinate resection should be performed conservatively.[12]

The turbinates are a recognized site of airflow sensation, and their loss may precipitate ENS.[13,14] I believe that poor regrowth of sensory nerves that are injured during turbinate surgery also takes place in ENS. The turbinates are recognized as a source of nerve growth factor.[15] The act of removing or damaging the source of this factor may predispose the nose to poor nerve healing and poor sensation to airflow. In a similar vein, the incidence rate of persistent hypoesthesia at the site of an inguinal herniorrhaphy is 26.4%.[16] Temporary local numbness follows any surgical incision. Unfortunately, for some patients, the hypoesthesia persists, which is particularly troubling in the nose. The nasal turbinates are rich in sensory receptors, and resecting a turbinate deprives the brain of their input and can damage a patient's quality of life.[17]

Alteration in the laminar airflow pattern after turbinate excision may also contribute to poor sensation and ENS. The loss of turbinate tissue disrupts airflow within the nose, which may be perceived as poor nasal breathing.[18] In the healthy nose, the air flows across the entire body of nasal mucosa; thus, there is vast trigeminal feedback sent from the receptors of the entire cavity. Proetz[2] and Grützenmacher et al[18] have shown that when, for example, an IT is removed, almost the entire airflow will converge into this enlarged empty cavity, along the nasal floor, and will not become elevated or deflected into

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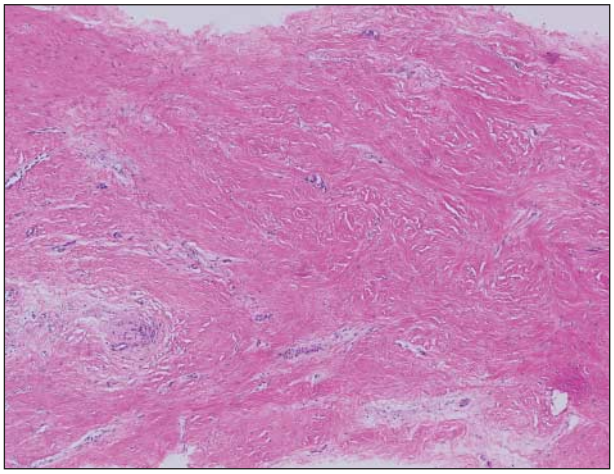

Figure 3. Histopathologic specimen of acellular dermis biopsied 6 months after implantation (hematoxylin-eosin, original magnification ×40).

the higher regions of the nose. Inspired air will go straight to the nasopharynx, "ignoring" (not stimulating or ventilating) the rest of the nose. This will manifest as a lack of trigeminal and olfactory mucosal stimulation; the subject will feel an abnormal sensation during breathing, as if the nose is partially anesthetized, partially obstructed, or simply absent. This is a very difficult sensation to describe. Although total turbinate excision is most frequently the cause of ENS, lesser procedures (eg, submucosal cautery, submucosal resection, cryosurgery) to reduce the turbinates may cause problems as well if performed in an overly aggressive manner. Two of the ENS-type patients in this series underwent laser turbinate reduction, which necessarily destroys overlying mucosa to reach the targeted underlying vascular tissue.

Therapy for patients with ENS centers on moisturization and an honest discussion of their concerns. If depression is evident, a referral for counseling is appropriate. Persistent pain symptoms may be best addressed by a pain therapy specialist. Continued treatment of underlying allergy and chronic sinusitis is important. It may be possible to offer to rebuild the internal nose. There are several goals to consider in that case: (1) to narrow the airway to provide more nasal resistance, (2) to allow the tissue to retain more moisture by reducing airflow, and (3) to deflect the airflow away from a somewhat insensate area toward "virgin" or unoperated tissue. Typically, the tissue high in the nasal vault is not manipulated during a surgical procedure involving turbinate reduction, so a corrective graft placed after the development of ENS would ideally direct the airflow superiorly (eg, in a case of ENS-IT).

Reflecting on nasal anatomy and physiologic characteristics can help to explain the symptoms of ENS and help direct us to devise repairs. The nose is more than just a conduit of air. It serves to condition the air before it reaches the lungs through filtration, heat regulation, and humidification. The nose provides more than 50% of the resistance in overall airflow[19] and conducts air and odorants toward the olfactory grooves. The IT directs airflow toward the middle meatus.[3,18] The turbinates themselves are bony structures with mucosal and submucosal covering. The IT has a great deal of capacitance vessels to alter its size and thus alter airflow. The MT has minimal capacitance tissue, but it has mucosal glands, harbors a small amount of olfactory nerve endings, and protects the sphenopalatine area.

The patient series detailed in this article indicates that a surgeon can intervene in ENS and provide some benefit to the patient. Although we cannot transplant mucosa from a donor or recruit schneiderian membrane from elsewhere in a patient's body, we can expand a patient's ambient tissue to simulate a turbinate. Nasal mucosa has limited elastin, so achieving true tissue expansion, compared with the facial skin, is difficult. However, we can balloon out a patient's mucosa into a space formerly occupied by turbinate tissue while creating minimal stretch. The material to use for such expansion and the location of placement become important factors to assess.

Various materials have been used for nasal mucosal tissue expansion, including autologous materials (eg, bone, cartilage, muscle, and fat) and biomaterials (eg, Teflon [DuPont, Parkersburg, West Virginia], Plastipore [Xomed, Jacksonville, Florida], Bone Source [Orthofix, Huntersville, North Carolina], Gore-Tex [Newark, Delaware], Alloderm [Life Cell]).[20,21] Rice[22] reported success with hydroxyapatite in a case report. Goldenberg et al[23] reported good outcomes in 8 of 8 patients using Plastipore for atrophic rhinitis. Friedman et al[24] and Moore and Kern[5] reported some success with acellular dermis (in 5 of 10 and 7 of 7 patients, respectively). Injectable materials are limited in the amount of bulk they can provide, they tend to resorb, and the nasal mucosa may rupture with a thick injection that spills and wastes the injection.

The small series of patients described herein demonstrates some improvement in patient symptoms with acellular dermis submucosal grafting. Acellular dermis becomes incorporated within the patient's tissue during the months following the implantation (in approximately 3-6 months depending on the size of the graft, estimated by observing initial shrinkage as the air pockets surrounding and within the graft are resorbed). The initial graft will appear to shrink as the tissue is incorporated, and then the graft appears to maintain a fairly stable size for years (personal observation). Sclafani et al[25] noted good longevity of acellular dermis sheets. As the acellular dermis becomes incorporated within the patient's body, the risk of infection from a foreign body becomes negligible. The histopathologic characteristics of a portion of incorporated acellular dermis show small blood vessels and robust collagen with embedded fibroblasts (**Figure 3**).

The location of an implant should ideally re-create the natural airflow patterns within the nose. The work of Grützenmacher et al[18] is a testament to the importance of maintaining anatomy for optimal airflow. This is the idea behind expanding an IT remnant to simulate a natural IT. Implanting the septum opposite the natural MT location is, in a fashion, simulating a "bolgerized" MT (a destabilized MT that is intentionally adhered to the septum for stability).[12]

Patients with ENS-IT without any IT remnant (or a minimal remnant) present a difficult reconstructive problem. On the one hand, the work of Friedman et al[24] suggests limited success with lateral wall augmentation (0 of 3 patients benefited from the procedure), and the nasolacri-

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mal duct might be obstructed. On the other hand, Mendonca et al[26] reported that their patients (7 of 7 patients with secondary atrophic rhinitis) did benefit from lateral wall implantation. The head of the natural IT enters into the nasal valve region where it directs airflow up toward the middle meatus.[3,18] A septal implant located anteriorly might function similarly. A lateral wall implant, which is tethered by the nasolacrimal duct and does not extend sufficiently to the anterior area, may not provide adequate relief. The ENS-both patients may benefit from a large septal implant bridging the regions of the IT and MT. It is critically important though, to perform a cotton test prior to implantation in an effort to temporarily alter the nasal airflow and assess the patient's subjective response; the patient's subjective sensations are the most important goal to maximize. I have been surprised several times as to the size and location of cotton placed during a cotton test that brought about a subjective improvement in breathing; cotton test findings are documented as the surgical plan to craft intraoperatively.

The ENS-type patients have IT and MT tissue, but they report symptoms consistent with ENS after IT surgery, and they improve with a cotton test. Their IT sensation to airflow is likely deficient after some sort of turbinate surgery (eg, laser reduction). Their IT can be expanded in its anterior half to provide relief. Thick acellular dermis can be partially rehydrated and cut into spearlike segments to pass into an IT submucosal pocket. A submucoperiosteal pocket is not feasible along the IT given the pockmarked IT bone.

The subjects in this series reported an improvement in their breathing sensation, nasal moisture content, sleep, and anxiety or depression. Patients who have pain as their predominant symptom do not seem to benefit much from implant therapy, whereas those with abnormal breathing sensations seem to benefit the most from implantation. It is not likely that patients can fully overcome ENS, but minimizing their symptoms can be of immense relief to them.

In conclusion, satisfying nasal breathing resides in a narrow defile between obstruction and inadequate nasal resistance. In the quest to reduce obstruction, patients may undergo too aggressive turbinate surgery and experience ENS as a result. Submucosal acellular dermis implantation may be beneficial in patients who experience ENS.

Recognition of ENS should lead otolaryngologists to avoid turbinate resection unless required for tumor excision, cerebrospinal leak repair, and so forth. Further research into multiple issues involving ENS is of paramount importance. The sensation of nasal airflow should be better mapped. The proper location of nasal reconstruction, in light of the surgical limitations and sensation issues, can be better identified. The most appropriate material(s) for reconstruction should be identified.

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